UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/457,926 | 12/08/1999 | BURTON G. CHRISTENSEN | P-061-R2 | 8221 |

22852 7590 03/28/2005

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

| EXAMINER | |
|---|---|
| SHIBUYA, MARK LANCE | |
| **ART UNIT** | **PAPER NUMBER** |
| 1639 | |

DATE MAILED: 03/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/457,926 | CHRISTENSEN ET AL. | |
| | Examiner | Art Unit | |
| | Mark L. Shibuya | 1639 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *01 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *41-46,49-51,53-55,57 and 58* is/are pending in the application.

4a) Of the above claim(s) *42,44-46,57 and 58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41,43,49-51 and 53-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/1/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.



JL

## DETAILED ACTION

1. Claims 41-46, 49-51, 53-55, 57 and 58 are pending. Claims 42, 44-46, 57 and 58 are withdrawn from consideration. Claims 41, 43, 49-51 and 53-55 are examined.

### *Withdrawn Rejections*

2. The rejection of claims 41-45, 49-51, 53-55, 57 and 58, under 35 USC 112, first paragraph, as failing to comply with the enablement requirement, is withdrawn, after consideration of applicant's Information Disclosure Statement, entered 12/1/2004; and applicant's arguments, entered 9/22/2004, and interview with the instant examiner and his supervisor, mailed 5/18/2004.

### *Continued Examination Under 37 CFR 1.114*

3. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/22/2004 has been entered.

4. The claims filed 9/22/2004, after final rejection, are considered herein.

### *Election/Restrictions*

5. The restriction and requirement for election of species, as set forth in the Requirement for Restriction/Election mailed 2/20/2001, and applicant's election of Group I, originally claims 41-55 and of species 2 of beta-lactam antibiotic, formula (b),

(claims 43, 53 and 54), Vancomycin, and the linkage set forth in claim 49, entered 3/19/2001, is maintained.

6. Claims 42, 44-46, 57 and 58 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected species, there being no allowable generic claim. See below rejection under 35 USC 103(a). Applicant is reminded that only upon the allowance of a generic claim are they entitled to consideration of claims to additional species which are written independent form or otherwise include all limitations of an allowed generic claim as provided by 37 CFR 1.141. See previous action for discussion of non-elected species claims.

***Information Disclosure Statement***

7. The Information Disclosure Statement, entered 12/01/2004, has been considered.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 41, 43, 49-51 and 53-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Truett (US 5,693,791; on PTO-1449) in view of Truett (US 6,437,119, IDS filed 12/1/2004, priority to May 7, 1998); and Boeckh et al (Antimicrob. Agents Chemother., 1988, Vol. 32, No. 1, pp. 92-95; of record) and Renoud-Grappin et al (Antiviral Chem. and Chemotherapy, Vol. 9, No.3, 1998, pp. 205-221, of record) and Staroske et al (Tet. Lett., 1998, Vol. 39; on PTO-1449).

**Truett, US 5,693,791**, teaches the "linking of diverse antibiotic moieties via difunctional organic compounds" (see column 1, lines 8-9). Specifically, dimers are taught having the structure A-L-B, where A and B are various antibiotic moieties (see "Summary", columns 1-6, especially column 1, lines 46-64). A variety of linkers and linkage chemistries are taught (see columns 25-32). The reference teaches that the linkage of two antibiotic moieties can create compounds of new activity (see column 1, lines 1-30) and that "two antibiotic moieties can be linked in which one is known to attack Gram positive bacteria and another to attack Gram negative bacteria" (see column 1, lines 27-30). Truett teaches a dimeric compound where one of the antibiotic moieties is ceftazidime (see column 3, line 7). Ceftazidime is a beta lactam antibiotic that reads on the elected species that is set forth in claim 53, see structure in the instant Figure 6B-2. Truett lacks the teaching of linking vancomycin with ceftazidime.

**Truett, US 6,437,119**, throughout the patent and abstract, teaches linking antibiotics by internal reactions to give three linked antibiotics for controlling infections via suppressing DNA replication, cell wall formation and protein synthesis. Truett, US 6,437,119, at col. 1, lines 12-21, col. 2, lies 26-34, col. 2, line 65-col. 3, line 47, and col.

26, lines 48-56, teach that making and using compounds having three antibiotic functionalities linked together, where a quinolone derivative is linked to a beta-lactam, which, in turn, is linked to vancomycin. Thus Truett, US 6,437,119 teaches linking a beta-lactam antibiotic to vancomycin in an antibiotic compound. Truett, US 6,437,119, is a continuation in part of US Application No. 09/304,715, filed 5/4/1999, and claims benefit of Provisional Application No. 60/084,586, filed 5/7/1998.

It was well known in the art at the time of filing to use combination therapy with vancomycin and ceftazidime. For example, **Boeckh et al** teach that this combination therapy is used to "cover a broad spectrum of gram positive and gram negative bacteria-- (see page 92, first paragraph). The reference teaches the pharmacokinetics of the combination of vancomycin and ceftazidime, administered to humans (see Abstract and Table 1), thus pharmaceutical compositions of the drugs are well known.

**Renoud-Grappin et al** teach that one way to achieve effective combination therapy is to covalently link two different drugs. See page 208, first column, first full paragraph of the reference, which describes using heterodimers for combination therapy linked "through an appropriate spacer, in an attempt to combine the inhibitory capacity" of two different classes of molecules. The reference also describes that one would attempt such an approach to span two binding sites on the target. Renoud-Grappin et al also discuss combining different drugs to "prevent the emergence of drug-resistant virus strains" and set forth three main reasons for combination therapy (see page 207, 2nd column, 2nd paragraph. It is recognized that the linked compounds of Renoud-Grappin et al (see, for example, Figure 4 of the reference) are anti-virals and

not antibiotics; however, it is the examiner's position that one of ordinary skill would recognize the relevance of preventing the emergence of drug-resistant strains for both classes of molecules since such was well established in the art.

Additionally, vancomycin dimers were also known in the art at the time of filing. **Staroske et al** discuss both "head-to-head" and "head-to-tail" dimers (see Figure 3) and that in "light of recent reports of vancomycin-resistant bacteria" there is a "strong incentive for the development of more potent antibiotics" (page 4917, bottom). The reference also teaches that dimeric vancomycin compounds exhibit improved antibacterial activity, see for example, page 4918, top. Specifically, the dimers of Staroske et al are linked from the amino terminus of one vancomycin moiety to the carboxy terminus of another (see Scheme 1, page 4919). The reference also contemplates linking of the vancomycin at the vancosamine moiety (see page 4920, last two paragraphs).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to link vancomycin and ceftazidime, based on the teaching of Truett, US 5,693,791, concerning the linking of diverse antibiotic moieties, and Truett US 6,437,119, where vancomycin and beta-lactam antibiotics are linked as part of a linked, three antibiotic compound, combined with the teaching of Boeckh et al to perform combination therapy using the drugs, the teaching of Renoud-Grappin concerning linking drugs to perform combination therapy and the teaching of Staroske et al concerning vancomycin dimers linked through the amino and carboxy terminus. Specifically, the references of Truett, US 5,693,791, teach that two antibiotics, one

known to attack Gram positive bacteria and another to attack Gram negative bacteria can be linked and the advantages of doing such, and Boeckh et al teach that vancomycin and ceftazidime fulfill these requirements. Furthermore, Truett US 6,437,119, teaches linking vancomycin and a beta-lactam as part of a three compound antibiotic. Renoud-Grappin teaches that one way to achieve effective combination therapy is to covalently link two different drugs. Finally, Staroske et al teach that vancomycin can be linked at specific linkage sites.

One of ordinary skill would have been motivated to covalently link vancomycin with ceftazidime to create a broad spectrum antibiotic compound to fight antibiotic resistant strains. Furthermore, it would have been obvious for one of ordinary skill in the art to have combined the compounds taught by the references of Truett, US 5,693,791 and Truett US 6,437,119, because said compounds are used for a common purpose, i.e., the treatment of bacterial infection. See In re Kerhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (stating: "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art" [citations omitted]); and MPEP 2144.06.

One of ordinary skill would also have had a reasonable expectation of success based on the fact that the references of Truett, US 5,693,791 and Truett US 6,437,119 and Staroske et al teach linking chemistry for vancomycin and beta-lactam compounds.

***Conclusion***

9. Claims 41, 43, 49-51 and 53-55 are rejected.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Shibuya whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark L. Shibuya
Examiner
Art Unit 1639

ms

PADMASHRI PONNALURI
PRIMARY EXAMINER